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| EXAMINER | |
|---|---|
| ZEMAN, ROBERT A | |
| ART UNIT | PAPER NUMBER |
| 1645 | |

| SHORTENED STATUTORY PERIOD OF RESPONSE | NOTIFICATION DATE | DELIVERY MODE |
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Notice of this Office communication was sent electronically on the above-indicated "Notification Date" and has a shortened statutory period for reply of 3 MONTHS from 01/26/2007.

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PTO-PAT-Email@rfem.com

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| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/759,345 | ROBINSON, DOUGLAS H. | |
| | Examiner | Art Unit | |
| | Robert A. Zeman | 1645 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *31 October 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *4-14,19-23,30 and 31* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *4-14,19-23,30 and 31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

The Appeal Brief filed on 10-31-2006 is acknowledged. In light of a careful review of the record, the finality of the previous Office action is withdrawn. Applicant's traversals of the pending rejections set forth in said brief are addressed below. Claims 4-14, 19-23 and 30-31 are pending.

### *Claim Rejections Withdrawn*

The rejection of claims 4-14, 19-23 and 30-31 under 35 U.S.C. 112, first paragraph, the specification, while being enabling for a method for isolating a bacterium comprising aseptically culturing retrovirally transformed human capillary microvascular endothelial cells (ATCC CRL 11655); subjecting said culture to an anaerobic culturing phase wherein said culture is exposed to oxygen conditions corresponding to an atmosphere containing of about 0 to 2% v/v oxygen for a period of between 18 and 24 hours; exposing said culture to oxygen conditions corresponding to an atmosphere containing greater than 2% v/v oxygen; subjecting said culture to an additional anaerobic culturing phase wherein said culture is exposed to oxygen conditions corresponding to an atmosphere containing of about 0 to 2% v/v oxygen for a period of between 18 and 24 hours; subjecting said culture to an additional aerobic culturing phase under aseptic culturing conditions and corresponding to an atmosphere containing greater than about 2% v/v oxygen; isolating a bacterium from the culture (either *Staphylococcus aureus* ATCC 55589, *Staphylococcus capitis* ATCC 55590, *Staphylococcus hemolyticus* ATCC 55592, *Staphylococcus epidermidis* ATTC 55591 or *Micrococcus luteus* ATCC 55588), does not reasonably provide enablement for methods for **producing** a bacterium that contains a eukaryotic and/or viral gene comprising

culturing virally-infected eukaryotic cells under low oxygen conditions is withdrawn in lieu of the enablement rejection set forth below.

The new matter rejection claim 30 based on the limitation "identifiable as a bacteria and contains a eukaryotic and/or viral gene" is withdrawn.

The rejection of claims 30 and 31 under 35 USC 112, second paragraph as being rendered vague and indefinite by the use of the phrase "under sterile conditions" is withdrawn

***Claim Rejections Maintained***

**35 USC § 101**

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The rejection of claims 4-14, 19-23 and 30 under 35 U.S.C. 101 is maintained for reasons of record. The claimed invention is not supported by either a credible asserted utility or a well-established utility, as the **disclosed invention is inoperative**. The rejection of claim 31 is withdrawn in lieu of the art rejection(s) set forth below.

The claims, while they do not explicitly recite the phrase "producing a bacterium", are, based on the specification, drawn to a method for **producing a bacterium** that contains a eukaryotic and/or viral gene, which comprises culturing virally infected eukaryotic cells under low oxygen conditions to produce a bacterium containing a eukaryotic and/or viral gene. The specification at page 9 indicates that the present invention provides a process for producing a bacteria containing at least one eukaryotic gene. The specification at page 9 further states "the process of the present invention, sometimes called *de novo* speciation, can be divided into the following stages:

(I) Culturing virally-infected eukaryotic cells under low oxygen conditions to **produce a bacterium** containing a eukaryotic and/or viral gene; and

(II) Selecting and replicating at least one such bacterium."

Accordingly, the claims and the specification call for a method for producing a bacterium containing a eukaryotic and/or viral gene, which comprises culturing virally-infected eukaryotic cells under low oxygen conditions to produce a bacterium containing a eukaryotic and/or viral gene whereby neither the bacterium nor the bacterial genome is introduced. Barron's Law Dictionary 3rd Edition defines *"de novo "* as "new, young, fresh; renewed, revived..." and Webster's II New Riverside Dictionary defines "speciation" as "the evolutionary process by which new species are formed." Therefore, Applicant is calling for the *de novo* "creation" of a new species and/or the "creation of a life form", i.e., the bacterium, from eukaryotes without the introduction of bacterial genes or the bacteria themselves. However, current knowledge of scientific principles maintains that prokaryotes and eukaryotes constitute separate and distinct life forms having many differences in structure and function. The most striking difference pertains to the presence or absence of a nucleus. That the only recognized process in the art for the acquisition of new traits is mutation is well settled. Moreover, the process of the acquisition of new traits is a slow process that requires so many changes that more than anaerobic cultivation for a few hours or even a few years is necessary. To the best of scientific knowledge, the evolution of first one-celled and then many-celled eukaryotes from one-celled prokaryotes is believed to have taken several million years and not a few hours or days. Likewise, it appears that Applicant is calling for the "spontaneous" production of a new bacterium without the introduction of the bacteria or the bacterial genome. It should be remembered that Louis Pasteur effectively disproved the principles of spontaneous generation at the end of the last century in historical experiments. Therefore, the specification fails to show a

clear correlation between culturing retrovirally infected animal cells in the amount of oxygen given and the "creation" (i.e., the production) of a new species of bacteria.

**Applicant argues:**

1. The Examiner has not applied the rejection to the claims as presently pending as the rejection refers to "a method of producing a bacterium" when said language does not appear in the instant claims.

2. The composition of claim 31 is not addressed in the rejection.

3. The examiner does dispute any of the statements in the specification regarding the utility of the cells produced by the claimed methods.

4. The instant claims recite a method comprised of a specific series of steps that provide a certain, clearly defined, type of cell (i.e. a cell identifiable as a bacteria and contains a eukaryotic and/or viral gene).

5. The specification contains working examples and experimental data that demonstrate the practice of the recited method steps provides the claimed cells and hence demonstrate the operability of the claimed method.

6. The Examiner does not even mention the experimental evidence of operability in the specification.

7. The amended claims overcome the deficiency in claim language noted by the board.

8. If the board was that based on the evidence of record the "recovered bacteria" of the claimed method were not due to contamination of a sterile starting culture, and that even if there were contaminants this does not account for the fact that said cells contained a eukaryotic and/or viral gene, the board is indicating that the process is operative.

9. It is the burden of the PTO to come forward with evidence that calls into question that calls into question the applicant's showing of operability of the claimed invention.

**Examiner Rebuts:**

With regard to Point 1, while they do not explicitly recite the phrase "producing a bacterium", are, based on the specification, drawn to a method for **producing a bacterium** that contains a eukaryotic and/or viral gene, which comprises culturing virally infected eukaryotic cells under low oxygen conditions to produce a bacterium containing a eukaryotic and/or viral gene. The specification at page 9 indicates that the present invention provides a process for producing a bacteria containing at least one eukaryotic gene. The specification at page 9 further states "the process of the present invention, sometimes called *de novo* speciation, can be divided into the following stages:

(I) Culturing virally-infected eukaryotic cells under low oxygen conditions to **produce a bacterium** containing a eukaryotic and/or viral gene; and

(II) Selecting and replicating at least one such bacterium."

Accordingly, the claims and the specification call for a method for producing a bacterium containing a eukaryotic and/or viral gene, which comprises culturing virally-infected eukaryotic cells under low oxygen conditions to produce a bacterium containing a eukaryotic and/or viral gene whereby neither the bacterium nor the bacterial genome is introduced. Barron's Law Dictionary 3rd Edition defines *"de novo "* as "new, young, fresh; renewed, revived..." and Webster's II New Riverside Dictionary defines "speciation" as "the evolutionary process by which new species are formed." Therefore, Applicant is calling for the *de novo* "creation" of a new species and/or the "creation of a life form", i.e., the bacterium, from eukaryotes without the introduction of bacterial genes or the bacteria themselves.

With regard to Points 2-3, claim 31 is not included in this rejection.

With regard to Point 4-6, the instant claims require the production of a cell identifiable as a bacterium wherein no bacteria or bacterial genome is introduced (purposely) into the culture. Current knowledge of scientific principles maintains that prokaryotes and eukaryotes constitute separate and distinct life forms having many differences in structure and function. The most striking differences pertain to the presence or absence of a nucleus and genomic organization. That the only recognized process in the art for the acquisition of new traits is mutation is well settled. Moreover, the process of the acquisition of new traits is a slow process that requires so many changes that more than anaerobic cultivation for a few hours or even a few years is necessary. To the best of scientific knowledge, the evolution of first one-celled and then many-celled eukaryotes from one-celled prokaryotes is believed to have taken several million years and not a few hours or days. Moreover, the specification is insufficient to disprove one of the basic tenets of modern science. Finally, it should be noted that the fact that Applicant does not specifically recite the terms "production" or "*de novo* creation of a species" does not obviate the fact that, in essence, that is what he is claiming. The instant claims require the generation of bacteria from a culture of virally infected eukaryotic cells where said bacteria are claimed to be neither present in the starting materials nor introduced during the method. Hence said bacteria are "produced" from the eukaryotic cells.

With regard to Point 7, the limitation "free of any overt microbiological contamination" is not commensurate with the limitation "uncontaminated by bacteria" referred to by the Board (see page 8 of Remand).

With regard to Point 8, the Board did not state that the evidence demonstrated that the claimed method steps would result in the production of "recovered bacteria containing a eukaryotic and/or viral gene. If fact, the Board clearly points out, that it was "unclear why the *B. lichenformis* "produced" (according the Steuer Declaration) was not screened for the presence of

a eukaryotic and/or viral gene as required by the claimed invention" (see page 9 of the Remand). Read in context, the Board clearly points out that the assertion that the bacteria was "produced" by the claimed method was made by Dr. Steuer and cannot be construed as indicating the claimed method steps are operative. Moreover, Applicant has provided no evidence, that the claimed method is operative. Even the Steuer Declaration cannot be relied upon by Applicant, as it provides no evidence that the bacteria he "produced" contained the requisite eukaryotic and/or viral gene.

With regard to Point 9, Applicant has not provided a showing of operability of the claimed invention, hence this rejection. Moreover, as pointed out by Applicant on page 12, of his brief, the PTO can make a rejection under 101 for inoperability when it has reason to doubt the objective truth of the statements contained in the written description. In this case, the fact that the claimed method runs contrary to modern scientific dogma is sufficient reason to "doubt the objective truth" of the statements contained in the specification.

As Applicant has failed to demonstrate that the execution of the claimed method steps would result in the **production of a bacterium** (i.e. cells identifiable as bacteria) **containing a eukaryotic and/or viral gene,** the rejection is maintained.

Claims 4-14, 19-23 and 30-31 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

The new matter rejection of claims 30 and 31 based on the limitation "free of any overt microbiological contamination..." is maintained for reasons of record.

**Applicant argues:**

1. The phrase is supported in the specification at pages 20 to 26.

Applicant's arguments have been fully considered and deemed non-persuasive. The limitation is drawn to any microbe (i.e. viral, bacterial, fungal, yeast etc) while the cited specification only uses said term with regard to bacteria fungi and mycoplasma only. Moreover, the term overt is only used with regard to bacteria. Consequently, the specification does not have support for the full breadth of the aforementioned limitation.

The new matter rejection of claims 30 and 31 based on the limitation "under sterile culturing conditions..." is maintained for reasons of record.

**Applicant argues:**

1. The phrase is supported in the specification at pages 9, lines 21-23; page 18, lines 17-23; page 18, line 31 to page 19, line 2; page 19, lines 4-7; page 19, lines 8-11; page 19, lines 16-18, page 23, lines 16-18; page 23, lines 21-24; page 23, lines 27-29 and page 24, lines 21-23.

Applicant's arguments have been fully considered and deemed non-persuasive. The cited portions of the specification describe items used in culturing which are sterile whereas said limitation is drawn to the conditions under which the cells are cultured.

The new matter rejection of claim 31 based on the limitation "one gene evolved from the genome of said eukaryotic cell" is maintained for reasons of record.

**Applicant argues:**

1. The specification discloses on page 7, lines 7-25, that the eukaryotic gene found on in the bacterium does not have to be identical to the gene present in the eukaryotic cell. Moreover, as a gene that changes can be said to "evolve", said disclosure provides support for the aforementioned limitation.

Applicant's arguments have been fully considered and deemed non-persuasive. Applicant's example regarding the development of antibiotic resistance describes the acquisition of a gene, not the evolution of a gene. Moreover, the term "evolved" suggests that the gene is functional which is not a limitation of the instant claims nor is it supported by specification.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

The rejection of claims 4-14, 19-23 and 30-31 rejected under 35 U.S.C. 112, second paragraph, as failing to set forth the subject matter which applicant(s) regard as their invention is maintained for reasons of record.

**Applicant argues:**

1. Applicant has consistently stated that his invention comprises a method whereby virally infected eukaryotic cells are cultured under alternating anaerobic and aerobic conditions which results in the production of cells that in many respects resemble bacteria, but contain a viral or eukaryotic gene.

Applicant's arguments have been fully considered and deemed non-persuasive. Again Applicant's summary of his invention is different than that put forth previously. There is a difference between "resembling a bacteria in many respects" and being a bacterium.

As outlined previously, evidence that claims 4-14, 19-23 and 30-31 fail(s) to correspond in scope with that which applicant(s) regard as the invention can be found in the reply filed 11-17-2003. In that paper, applicant has stated that the instant claims are drawn to "methods for **producing a bacterium** that contains a eukaryotic and/or viral gene which comprises culturing virally-infected eukaryotic cells under low-oxygen conditions and this statement indicates that the invention is different from what is defined in the claim(s) because said statement requires that the genome of the "produced" bacteria is prokaryotic in nature suggesting that the claimed method induces a "de-evolution" of the eukaryotic cell. The instant claims are drawn to cells identifiable as a bacteria and containing a eukaryotic and/or viral gene. Said claims are drawn to any cell that has the phenotype of a prokaryote regardless of its genomic organization (i.e. eukaryotic vs. prokaryotic genome) not a bacteria and containing a eukaryotic and/or viral gene.

Claims 4-14-, 19-23 and 30-31 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The rejection of claim 31 under 35 U.S.C. 112, second paragraph, as being rendered vague and indefinite by the use of the phrase "gene evolved from the genome of said eukaryotic cell" is maintained for reasons of record. It is unclear what is meant by said phrase, as it is not

explicitly defined in the specification. Consequently, it is impossible to determine the metes and bounds of the claimed invention.

**Applicant argues:**

1. Said term has a readily identifiable meaning.

Applicant's argument has been fully considered and deemed non-persuasive. As the specification fails to set forth what constitutes an "evolved" gene, said term does not have a readily identifiable meaning.

***New Grounds of Rejection***

***35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 4-14, 19-23 and 30-31 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention without undue experimentation.

Undue experimentation is a conclusion reached by weighing the noted factual considerations set forth below as seen in *In re* Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). A conclusion of lack of enablement means that, based on the evidence regarding each of the factors below, the specification, at the time the application was filed, would

not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation.

The factors include, but are not limited to:

1. The breadth of the claims,
2. The nature of the invention,
3. The state of the prior art,
4. The level of one of ordinary skill,
5. The level of predictability in the art,
6. The amount of direction provided by the inventor,
7. The existence of working examples, and
8. The quantity of experimentation needed to make and/or use the invention based on the content of the disclosure.

The applicable factors will be addressed below.

**Nature of the Invention**

The instant invention is drawn to a method of culturing virally infected eukaryotic cells comprising subjecting said culture to an anaerobic culturing phase wherein said culture is exposed to oxygen conditions corresponding to an atmosphere containing of about 0 to 2% v/v oxygen for a period of between 18 and 24 hours; exposing said culture to oxygen conditions corresponding to an atmosphere containing greater than 2% v/v oxygen; subjecting said culture to an additional anaerobic culturing phase wherein said culture is exposed to oxygen conditions corresponding to an atmosphere containing of about 0 to 2% v/v oxygen for a period of between 18 and 24 hours; subjecting said culture to an additional aerobic culturing phase under aseptic culturing conditions and corresponding to an atmosphere containing greater than about 2% v/v oxygen; isolating/identifying a bacterium from the culture. Moreover, the instant claims require the generation of bacteria from a culture of virally infected eukaryotic cells where said bacteria are claimed to

be neither present in the starting materials nor introduced during the method. Hence said bacteria "produced" from the eukaryotic cells.

**Breadth of Claims**

The instant claims encompass the culturing of any virally infected eukaryotic cell giving rise to the production of any bacterial cell comprising a viral and/or eukaryotic gene.

**State of the Art/Level of Predictability in the Art**

The art is silent with regard to transforming virally infected eukaryotic cells into bacteria by exposing said eukaryotic cells to anaerobic and microaerophilic conditions. Moreover, as the instant claims are drawn to methods that run contrary to accepted scientific theory, the prior art provides no means of predicting what virus/eukaryotic cell combinations would give rise the recited bacteria when exposed the recited culture conditions.

**Working Examples/Guidance in the Specification/Undue Experimentation**

It does not appear that the claimed method would be suitable for the production of bacteria from any and **all virally infected eukaryotic cells**. From the record of the written disclosure specific bacteria were obtained by the cultivation of the specific cell lines in specific media. In view of the specific nutritional requirements of different types of "cell cultures" and of different bacteria, there is no reasonable expectation that any and all types of bacteria may be "produced" or even isolated from any and all cell cultures by the procedure claimed. For example, any anaerobic bacteria would be destroyed upon exposure to aerobic conditions. In addition, the claims lack

specific method steps for the recovery of the bacteria. Thus, it is unclear that the claimed method would be suitable for the recovery of any and all bacteria, a few of which may be present, but not detectable by certain means. Moreover, one of ordinary skill in the art would not reasonably expect any and all possible viral infected eukaryotic cell cultures to harbor or to be contaminated by bacteria, especially if stringent aseptic technique is used. In this respect, it is apparent that only very specific sources of cell cultures would be suitable for the claimed invention. However, the specification provides insufficient guidance for one skilled in the art to obtain such cell cultures. In addition, it is unclear what precautions were taken in the instant case to assure that the bacteria harvested are not incidental contaminants inadvertently introduced into the cell culture. Moreover, it is well known in the art that bacteria are common cell culture contaminants (see Freshney "Culture of Animal Cells: A Manual of Basic Technique 2nd Edition", Alan R. Liss, Inc., New York, 1984, pages 207-208). Thus, there is no clear correlation between the instant method of culturing and the generation of new strains of bacteria.

It is also apparent that the claimed method is unpredictable and would appear to depend on the type of cell cultured and the type of virus employed. It is unclear how the cell culture is chosen to have a reasonable a degree of certainty that bacteria as required can be "produced", in the absence of positive steps to modify existing bacteria and to assure the survival of the cell culture for a time period. What step actually produces the bacterium? Is it sufficient for any bacterium to be grown in any virally infected eukaryotic cell in order to acquire both eukaryotic and viral genes? Accordingly, in view of the lack of guidance, the claims as written constitute nothing more than an invitation to experiment.

The present invention would also require undue experimentation to practice in view of the unpredictable completion of the culturing steps. The specification indicates that the cultured cells under anaerobic conditions results in the death of the eukaryotic cells. However, the claims include no such limitation, accordingly, it is unclear if the eukaryotic cells are to be living or dead at this point. Likewise, the specification indicates that culturing under low oxygen conditions results in the production of the bacterium. However, what actual step leads to the production of the bacterium? Where are the genetic elements necessary for this event to occur (i.e., what is the origin of the bacteria)? While it is true that bacteria are a frequent contaminant of a cell culture, it is not apparent that the purpose of the present invention is to recover contaminants. Likewise, which eukaryotic cells should one use, and what virus should be employed?

Additionally, it is unclear how one of skill in the art would determine and assure that the actual viral and/or eukaryotic genes are indeed intact genes picked up rather than random fragments thereof. The cell line of the specification uses retrovirally-infected cells. However, by convention, retroviral genes have been found to be ubiquitous in all types of different organisms, such that virtually any cell culture would reasonably be expected to have at least pieces of DNA from these viruses. In addition, it is well known in the art that many animal species harbor endogenous retroviral genes. However, it is unclear how one skilled in the art would determine that the cell culture has these "genes" without undue experimentation. Regarding the genes or fragments that are to be present in the bacteria, it is unclear whether such pieces are to be stably incorporated into the genome and that proteins will be expressed by them. For DNA to integrate, homologous recombination is needed, such that the respective sequences must already be present in the bacteria. Therefore, it is unclear whether a stable product is produced.

In view of the lack of guidance provided by the disclosure, the limited number of working examples, the state of the art, the breadth of the claims, and the unpredictably nature of the invention, it would take an undue amount of experimentation to practice the claimed invention.

Applicant's arguments, presented in his appeal brief, are addressed below to the degree they read on the instant rejection.

**Applicant argues:**

1. The claims do not recite "production of bacteria". By characterizing the claimed methods as methods of "producing a bacterium" the examiner has ignored the clear and unambiguous meaning of the claim language and substituted language from the specification that alters its meaning without providing any textual reference that invites that alteration.

2. The claims do not require the isolation of "any and all bacteria" from "any and all" virally infected cells. The standard of enablement does not require the invention function in each and every embodiment encompassed by the claims.

3. The fact pattern of *Ajinomoto Co., Inc. v. Archer-Daniels-Midland Co.* is germane as it requires the selection of particular starting materials from a diverse universe of cell lines and screening the modified cells to determine whether or not the desired result had been achieved. In the instant case: the characterization and identification of the cell produced thereby are all within the ordinary skill in the art.

4. The evidence of record shows within a reasonable degree of scientific certainty that the methods as presently claimed provide cells that are identifiable as bacteria and contain a eukaryotic and/or viral gene (See Example 1, Comparative Example D, Example 4, Comparative Example 4/A, Example 5, Comparative Example 1/B, 1/C, 1D and 2A

5. The Declaration of Dr. Steuer provides additional evidence of the efficacy of the claimed method.

6. The Examiner has provided no evidence that rebuts or impeaches the credibility of the Final Report or Dr. Steuer's declaration

7. No undue experimentation is required to practice the instant invention as it is not necessary to know or understand the mechanism by which the claimed method works.

8. Similar claims have been allowed in Europe.

**Examiner Rebuts**

With regard to Point 1, the instant claims recite no preamble to describe the goal of the recited method. Moreover, said method steps are disclosed in the instant specification only in the context of a method of producing bacteria. Contrary to Applicant's assertion, the Examiner is not "ignoring" the claim language, but merely interpreting vague claim language in light of the specification. Moreover, as the specification provides no support for any method other than "producing a bacteria" utilizing the recited method steps this does not constitute an "improper construction of claims" and any amendment to said claims claiming any other "goal" would constitute impermissible new matter. The instant claims require the generation of bacteria from a culture of virally infected eukaryotic cells where said bacteria are claimed to be neither present in the starting materials nor introduced during the method. Hence said bacteria "produced" from the eukaryotic cells.

With regard to Point 2, as pointed out by Applicant on page 15 of his Appeal Brief, the enablement requirement is satisfied when the specification, combined with the knowledge of a person of ordinary skill in the art, permits one to practice the invention **without undue experimentation.** *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) states, "The amount of guidance or direction needed to enable the invention **is inversely related to the**

**amount of knowledge in the state of the art as well as the predictability in the art."** "The "amount of guidance or direction" refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature of the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to be explicitly stated in the specification. In contrast, **if little is known in the prior art about the nature of the invention** and the art is unpredictable, the specification would need more detail as to how to make and use the invention in order to be enabling" (MPEP 2164.03). The MPEP further states that physiological activity can be considered inherently unpredictable. **Thus, Applicant assumes a certain burden in establishing that inventions involving physiological activity are enabled**.

With regard to Point 3, while the actual culturing of a cell preparation is within the ordinary skill in the art, the ability to select starting material (i.e. virally infected eukaryotic cells that can be transformed into bacteria) is not (see above).

With regard to Point 4, the cells of Example 1, Comparative Example D, Example 4 and Example 4/A were not shown to have either a eukaryotic or viral gene as required by the instant claims and hence cannot be used as a support for the enablement of the instant claims. Moreover, the cells of Example 5 were shown to have "bacteria-like" morphology. This does not correlate to being identified as a bacterium. Finally, Comparative Example 1/B, 1/C, 1/D and 2A do not disclose the generation of cells identifiable as bacteria containing a eukaryotic and/or viral gene as required by the instant claim. .

With regard to Point 5, the declaration of Dr. Steuer is not persuasive as the cells "obtained" in his experiments were not shown to have either a eukaryotic or viral gene.

With regard to Point 6, *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) states, "The amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability in the art." "The "amount of guidance or direction" refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature of the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to be explicitly stated in the specification. In contrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as to how to make and use the invention in order to be enabling" (MPEP 2164.03). The MPEP further states that physiological activity can be considered inherently unpredictable. **Thus, Applicant assumes a certain burden in establishing that inventions involving physiological activity are enabled.** This is a burden that has not been met by Applicant. Contrary to his assertion, the Examples in the specification, the Final report, and the Steuer declaration do not provide support for Applicant's claim of enablement (see reasons above). Moreover, as the instant claims are drawn to devolution of a eukaryote into a prokaryote, no references can be cited by the Examiner, as said process runs contrary to accepted tenets of modern science.

Applicant should also take note that in assessing the weight to be given expert testimony, the examiner may properly consider, among other things, 1) the nature of the fact sought to be established, 2) the strength of any opposing evidence, 3) the interest of the expert in the outcome of the case, and 4) the presence or absence of factual support for the expert's opinion. See *Ex parte Simpson*, 61 USPQ2d 1009 (BPAI 2001), *Cf. Redac Int'l. Ltd. v. Lotus Development Corp.*,

81 F.3d 1576, 38 USPQ2d 1665 (Fed. Cir. 1996), *Paragon Podiatry Lab., Inc. v. KLM Lab., Inc.*, 948 F.2d 1182, 25 USPQ2d 1561, (Fed. Cir. 1993).

With regard to Point 7, while Applicant is correct that one does not necessarily have to understand the mechanisms by which a given process works in order to be enabled, one needs to know the phenotype/genotype of the eukaryotic cells that would give rise to claimed bacteria. Since there is nothing the art on which the practitioner can rely, he is necessarily limited to the disclosure within the specification. As the specification provides no examples of the production of the claimed cells (i.e. cells identifiable as bacteria), the practitioner has no means of predicting which (if any) eukaryotic cell/virus combinations would give rise to the claimed bacterial cell. It should be noted that the cells disclosed in Example 5 of the specification merely have "bacteria-like morphology" and don't rise to the level of being classified as bacteria.

With regard to Point 8, what was or wasn't allowed in Europe has no bearing on the prosecution of the instant application. U.S. patent applications are examined under the statutes and practices of the United States not the EPO.

Claim 31 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Applicant has amended the claim to recite "a pleiomorphic cell..." This phrase does not appear in the specification, or original claims as filed. Said phrase encompasses all pleiomorphic

cells and the specification only refers to pleiomorphic bacteria. Therefore this limitation is new matter.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 31 is rejected under 35 U.S.C. 102(b) as being anticipated by Pilarski et al. (Hematolo. Oncol. Clin. North. Amer. 1192, Vol. 6(2), pages 297-322)

Pilarski et al. discloses a population of highly pleiomorphic B cells (see abstract). As the B cells were taken from human multiple myeloma patients they would necessarily contain genes evolved from eukaryotes. Although Pilarski et al. disclose the same product they do not disclose the claimed method of making. However, it should be noted that the instant claim constitutes a Product-by-Process type claim. In Product-by-Process type claims, the process of producing the product is given no patentable weight since it does not impart novelty to a product when the product is taught by the prior art. See *In re Thorpe*, 227 USPQ 964 (CAFC 1985); *In re Marosi*, 218 USPQ 289, 292-293 (CAFC 1983) and *In re Brown*, 173 USPQ 685 (CCPA 1972). Consequently, even if a particular process used to prepare a product is novel and unobvious over the prior art, the product *per se*, even when limited to the particular process, is unpatentable over the same product taught in by the prior art. See *In re King*, 107 F.2d 618, 620, 43 USPQ 400, 402 (CCPA 1939); *In re Merz*, 97 F.2d 599, 601, 38 USPQ 143-145 (CCPA 1938); *In re Bergy*, 563

F.2d 1031, 1035, 195 USPQ 344, 348 (CCPA 1977) *vacated* 438 US 902 (1978); and *United States v. Ciba-Geigy Corp.*, 508 F. Supp. 1157, 1171, 211 USPQ 529, 543 (DNJ 1979). Finally, since the Patent Office does not have the facilities for examining and comparing Applicant's composition with the compositions of the prior art reference, the burden is upon Applicant to show a distinction between the material, structural and functional characteristics of the claimed composition and the composition of the prior art. See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977).

***Conclusion***

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert A. Zeman whose telephone number is (571) 272-0866. The examiner can normally be reached on Monday- Thursday, 7am -5:30 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on (571) 272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov.

Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

ROBERT A. ZEMAN
PRIMARY EXAMINER

January 17, 2007

JEFFREY SIEW
SUPERVISORY PATENT EXAMINER